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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/569,905	01/03/2007	Chad E. Kennedy	AZTE:026US	6537

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EXAMINER	
RUSSEL, JEFFREY E	
ART UNIT	**PAPER NUMBER**
1654	
MAIL DATE	**DELIVERY MODE**
10/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/569,905	KENNEDY ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *9-14* is/are allowed.

6)☒ Claim(s) *1,2,4,6-8,15-23,27 and 28* is/are rejected.

7)☒ Claim(s) *3,5 and 24-26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 February 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20060227*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. Applicant's election without traverse of the invention of Group I, claims 1-28, in the reply filed on August 11, 2008 is acknowledged.

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The declaration filed January 3, 2007 is defective because: It was not executed in accordance with either 37 CFR 1.66 or 1.68. MPEP 605.04(a) (see page 600-54, column 2, first paragraph - Rev. 7, July 2008) states that "Where individual declarations are executed, they must be submitted as individual declarations rather than combined into one declaration (by combining the signature pages)." Note that there are two signature pages designated "Page 2 of 3" in the submitted declaration, each page signed by a different inventor.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons:

The examiner has been unable to locate a paper copy of the Sequence Listing in the Image File Wrapper for this application. A copy of the sequence listing is not present in the WO/PCT publication of the international application upon which this national stage application is based, and was not present in the international application at the time the written opinion was prepared.

Applicant must provide a (substitute) paper copy of the Sequence Listing as well as an amendment directing its entry into the specification, and a statement that the content of the paper and computer readable copies are the same and include no new matter as required by 37 CFR

1.825(a) and (b). It is not necessary to re-submit a computer readable copy of the Sequence Listing.

4. The drawings are objected to because in Figure 2, the label "Fig. 2" is printed over some text, with the result that neither is legible. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

5. The disclosure is objected to because of the following informalities: At page 4, paragraph [0019] refers to a Figure 5e, which figure does not appear in the application papers. It is believed that "5e" should be changed to "5d". Appropriate correction is required.

6. Claims 7, 8, 15-21, 27, and 28 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claims 7 and 8, the "further comprises" language is

unclear. It is not clear if the second peptide comprises an RGD sequence and additionally comprises another CRGDSP/CRGDSPC sequence, or if the CRGDSP/CRGDSPC sequences themselves satisfy the requirement for an RGD sequence. There is no antecedent basis in the claims for the phrase "the conjugated peptide" at claim 15, line 1. It is not clear if Applicants intend to refer to one (or both) of the two peptides mentioned in the independent claim, or if Applicants intend to refer to the conjugated "dextran", which is recited at claim 9, lines 5 and 6. Claim 15 is indefinite because it states that "the conjugated peptide" (sic?) is "in higher proportion" than the acryloylated dextran. However, the claim does not state with respect to what the proportions are to be determined (e.g., with respect to each other, with respect to some other unidentified substance, or with respect to the total components present in the hydrogel), and does not state upon what basis (e.g., weight, mole, or volume) the proportions are to be determined. There is no antecedent basis in the claim for the phrases "the dextran mixture" at claim 16, line 7, and "the mixture" at claim 16, line 10. Note that there are at least two dextran combinations/mixtures mentioned prior to step d (see step b and step c), and that the provided dextran of step a is itself inherently a mixture of dextrans having different molecular weights. There is no antecedent basis in the claims for the phrase "the solution" at claim 18, line 2. Claim 18 is also indefinite because it states that the solution is to be "completely dissolved", but does not state in what the solution is to be completely dissolved. It is also possible that it is the dextran or the glycidyl methacrylate dextran product of step b, rather than a solution, which is to be completely dissolved, but again it would still be unclear as to in what the dextran or glycidyl methacrylate dextran product is to be dissolved. Note that no component of step b is identified as a solvent, or is required to be present in proportions such that it would act as a solvent. There

is no antecedent basis in the claims for the phrases "the mixing step", "the solution", and "the reaction" in claim 19. Claim 20 is unclear because it states that the acryloylated dextran is to be dialyzed after step c. No mention is made of dialyzing the glycidyl methacrylate dextran. However, because after step c, the acryloylated dextran and the glycidyl methacrylate dextran have been combined, it is not clear that the acryloylated dextran can be dialyzed without also dialyzing the glycidyl methacrylate dextran. It is possible that claim 20 incorrectly identifies the point during the claimed method when the acryloylated dextran is dialyzed. There is no antecedent basis in the claims for the phrases "the content" and "the conjugated dextran" in claim 21. Claim 21 is also indefinite because it states that the content of the conjugated dextran is greater than the content of acryloylated dextran; however, the claim does not state in what intermediate product or final product of the claimed method the content of the two components is to be determined, and the claim does not state upon what basis, e.g., weight, mole, or volume, the contents of the two components are to be determined. In claims 27 and 28, the "further comprises" language is unclear. It is not clear if the second peptide comprises an RGD sequence and additionally comprises another CRGDSP/CRGDSPC sequence, or if the CRGDSP/CRGDSPC sequences themselves satisfy the requirement for an RGD sequence.

7. Claims 1-8 and 22-28 are objected to because of the following informalities: Claim 1, line 3, refers to the cell-attracting peptide as "the other", whereas claim 6 refers to this peptide as "the second" peptide. Claim terminology needs to be standardized. Claim 22, line 2, refers to the cell-attracting peptide as "the other", whereas claim 26 refers to this peptide as "the second" peptide. Claim terminology needs to be standardized. Appropriate correction is required.

8. Claims 1 and 6-8 are not deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of provisional application 60/499,634 because the provisional application, under the test of 35 U.S.C. 112, first paragraph, does not disclose matrices in general (the disclosure of the provisional application is limited to hydrogels made from dextran), does not disclose covalent linkage of a cell-attracting peptide, and does not disclose cell-attracting peptides which comprise RGD, CRGDSP, or CRGDSPC.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

10. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Lee (U.S. Patent No. 5,763,399). Lee teaches a biodegradable matrix formed from human albumin-heparin conjugates to which is covalently attached human growth hormone. See Example 1. After implantation, the matrix is infiltrated by fibroblasts. See, e.g., column 4, lines 7-9 and 29-31, and column 6, lines 36-40. The human albumin of Lee corresponds to Applicants' first peptide cleavable by natural proteases; the heparin of Lee corresponds to Applicants' matrix; and the human growth hormone of Lee corresponds to Applicants' cell-attracting peptide (i.e. human growth hormone will attract cells which express receptors for the hGH).

11. Claims 2, 4, 22, and 23 are rejected under 35 U.S.C. 103(a) as being obvious over Lee (U.S. Patent No. 5,763,399). Application of Lee is the same as in the above rejection of claim 1. Lee does not teach a biodegradable matrix formed from a human albumin-dextran conjugate. However, Lee does teach that mixtures of polymers can be used to form the biodegradable matrix, and that preferred polymers include albumin, heparin, and dextran. See column 6, lines 52-56. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to substitute dextran for the heparin in the human albumin-heparin conjugates of Example 1 of Lee, because Lee teaches dextran to be a preferred polymer for forming the biodegradable matrices, because Lee teaches that dextran can be used in combination with other polymers, including albumin, to form biodegradable matrices, and

because the substitution of one known equivalent for another with only the expected result that a biodegradable matrix capable of inducing cell migration is formed is prima facie obvious. While Lee does not teach a molecular weight for the dextran to be used in his biodegradable matrices, it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal molecular weights for the dextran of Lee, because molecular weight is an art-recognized result-effective variable which is routinely determined and optimized in chemical and pharmaceutical arts involving polymers.

12. Claims 1, 6, and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by the Lutolf et al article (Nature Biotechnology, Vol. 21, pages 513-518). The Lutolf et al article teaches PEG-based hydrogels comprising pendent oligopeptide ligands for cell adhesion (C-RGDSP) and matrix metalloproteinase substrates as linkers between PEG chains. The hydrogels are used as cell-ingrowth matrices for in situ bone regeneration. See, e.g., the Abstract and Figure 1.

13. Claims 9-14 are allowed.

Claims 3, 5, and 24-26 would be allowable if rewritten to overcome the claim objections set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Claims 15-21 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.

Claims 8, 27, and 28 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, and the claim objections set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Lee (U.S. Patent No. 5,763,399), applied in the above prior art rejections, does not provide any motivation or other type of suggestion to use glycidyl methacrylate dextran, acryloylated dextran, or peptides comprising the specifically claimed amino acid sequences, in forming his biodegradable matrices.

The Lutolf et al article (Nature Biotechnology, Vol. 21, pages 513-518), applied in the above prior art rejection, does not provide any motivation or other type of suggestion to use dextran in place of the PEG in preparing hydrogels. With respect to instant claim 5, the prior art of record does not teach or suggest peptides comprising the claimed sequence. With respect to instant claim 8, the prior art of record teaches peptides comprising the claimed sequence as cell adhesion inhibitors, which does not provide any motivation or other type of suggestion for their use as cell-attracting peptides in the hydrogels of the Lutolf et al article.

Silver et al (U.S. Patent No. 4,970,298) is cited as art of interest, being essentially duplicative of Lee (U.S. Patent No. 5,763,399) applied above. See, e.g., column 6, lines 5-9, of Silver et al.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications

such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jeffrey E. Russel/
Primary Examiner, Art Unit 1654

JRussel
October 9, 2008